UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte PETER M. PRICE,
JUDIT MEGYESI, and
ROBERT SAFIRSTEIN

Appeal No. 2005-1073
Application No. 09/881,635

ON BRIEF

Before SCHEINER, GRIMES, and GREEN, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This appeal involves claims to treating kidney disease by reducing expression of the p21 gene. The examiner has rejected the claims on the basis that the specification is not enabling. We have jurisdiction under 35 U.S.C. § 134. We affirm.

Background

"The removal of substantial amounts of renal tissue is followed by a progressive decline in renal function. Glomerular hypertrophy occurs early in response to this ablation and is accompanied by short-term increases in glomerular filtration. These [changes] . . .are thought to be maladaptive and to influence the progression to end

stage renal disease[, although] . . . there is no established causal link between these events and the progressive nature of the renal disease." Specification, page 1.

"Acute short-term stress in the kidney provokes . . . expression of several genes, including the cyclin-dependent kinase (cdk) inhibitor p21. . . . The p21 protein acts as an inhibitor of cyclin dependent kinase activity and effectively stops cell-cycle progression." Page 3. "Chronic, long-term stress could provoke sustained expression of p21 and . . . such expression could influence renal function and morphology. Controlling p21 function may ameliorate or even prevent progressive end-stage renal disease." Pages 3-4.

The specification discloses "a method for treating or preventing a pathophysiological state of an organ in an individual wherein said state is characterized by an undesirable level of cyclin-dependent kinase inhibitor activity in said organ, comprising the step of regulating the expression of the p21 gene in said organ of said individual. . . . In one aspect of this embodiment the regulation of the expression of p21 results in the reduction or elimination of p21 expression. Preferably, reduction or elimination o[f] p21 expression is performed by a technique[ ] such as drug therapy, genetic manipulation, antisense DNA, etc." Pages 8-9.

Discussion

1. Claim construction

Claims 1, 3, 5, 6, and 8 are pending. According to Appellants, claims 6 and 8 stand or fall separately from claims 1, 3, and 5. See the Appeal Brief, pages 5-6. However, Appellants' brief presents no arguments to show the enablement of claim 6 separately from that of claim 1. See (then-applicable) 37 CFR § 1.192(c)(7). Since

Appellants have not separately argued the claims, all of the rejected claims will stand or fall together.

We will focus on claim 1, the broadest claim on appeal, which reads as follows:

1. A method for treating or preventing a pathophysiological state of a kidney in an individual, wherein said state is characterized by an undesirable level of cyclin-dependent kinase inhibitor activity in said kidney, comprising the step of reducing or eliminating the expression of the p21 gene in said kidney of said individual.

Thus, claim 1 is directed to a method comprising reducing or eliminating expression of p21 in a kidney, in vivo, in order to treat or prevent a "pathophysiological state."

2. Enablement

The examiner rejected claims 1, 3, 5, 6, and 8, all of the claims remaining, under 35 U.S.C. § 112, first paragraph, on the basis that the specification does not enable those skilled in the art to practice the claimed method without undue experimentation. The examiner considered many of the factors set out in In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), and found that

- the claims are very broad, in that they encompass treating or preventing a variety of pathological states using any compound that reduces or eliminates p21 expression;
- the relevant art considered gene therapy methods and antisense methods to be unpredictable;
- the specification provides no working examples showing reduction or elimination of p21 expression in an animal expressing p21;
- the specification does not disclose any specific molecules that can be administered to an animal to eliminate p21 expression; and
- an extremely large quantity of experimentation would be required, including "the identification of therapeutic molecules . . .[,] making and testing the therapeutic molecules and testing the therapeutic molecules in vitro, followed

> by testing in animal models to show that the treatment can overcome the problems recognized in the art.

See the Examiner's Answer, pages 5-6. The examiner concluded that "the amount of additional experimentation required to make and use the invention is considered to be undue." Id., page 6.

We agree with the examiner's analysis and his conclusion.

Appellants argue that the "specification discloses experiments employing partial renal ablation as a model of chronic renal failure," that the "experimental results disclosed indicate that p21 has a critical role in the functional and morphological consequences subsequent to the stress of renal ablation," and that "the in vivo mouse model experiments disclosed allow a reasonable prediction that reducing or eliminating p21 gene expression will be able to ameliorate or prevent the effects of acute renal stress or chronic renal failure." Appeal Brief, pages 8-9.

These arguments are not persuasive because they do not address the experimentation required to practice the claimed method. That is, the mouse model used in the specification may well suggest to those skilled in the art that reducing or eliminating p21 expression in vivo might aid in treating certain kidney disorders. However, as the examiner has pointed out, the mice used in the specification's example were genetically bred to lack any p21 expression; therefore, the specification's working example does not involve reducing or eliminating expression of p21 in individuals that express p21.

Appellants also argue that "there was ongoing research and development of gene therapy and antisense methods at the time of filing of the present application." Id.,

page 11 (citing Crystal[1] and Branch[2]). Appellants conclude that "in view of the state of the art, . . . the level of development and skill in the art is sufficient to allow the practice of the present claims without undue experimentation." Id., pages 11-12.

We do not agree that the state of the art makes up for the lack of substantive disclosure in the specification. Appellants cite Crystal for its disclosure that "human gene transfer is feasible" and has been carried out in several ex vivo and in vivo studies. We agree with the examiner, however, that these disclosures have little relevance to the instant claims. As the examiner pointed out, Crystal's disclosure relates to restoring expression of a given gene in cells that lack expression of that gene; to practice the instant claims using method discussed by Crystal, "one of skill in the art would have to know which gene would express a protein that reduces or eliminates p21 expression in kidney cells. The specification does not describe any [such] genes." Examiner's Answer, pages 11-12.

With regard to Branch, Appellants cite the single passage that states "Today's peak specificity, whatever it is, will almost certainly rise as current strategies are optimized and advances in nucleic acid chemistry bring derivatives with fewer side effects." Appeal Brief, page 12. Appellants provide no further explanation of how this passage helps their case. We have reviewed the full reference and find that it supports the examiner's position, not Appellants'.

Branch discloses that antisense and ribozyme strategies have been proposed for reducing or eliminating expression of a specific gene. Page 45, left-hand column.

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[1] Crystal, "Transfer of genes to humans: Early lessons and obstacles to success," Science, Vol. 270, pp. 404-410 (1995).
[2] Branch, "A good antisense molecule is hard to find," TIBS, Vol. 23, pp. 45-50 (1998).

Branch teaches, however, that antisense approaches have been plagued by unpredictable "'non-antisense' effects, which occur when a nucleic acid drug acts on some molecule other than its intended target." Page 45, center column. "[N]on-antisense effects muddy the waters. They make true antisense drugs more difficult to design and harder to commercialize. Furthermore, they can be a source of toxicity." Page 46, center column, first paragraph. With regard to ribozymes, Branch teaches that "it remains to be determined" whether the properties of ribozymes can be optimized such that they will specifically cleave mRNA from a targeted gene; "[i]t will not be surprising if bioengineered ribozymes are incapable of knocking out single genes." Page 48, center column, full paragraph. Finally, Branch teaches that the folding patterns of target RNAs in vivo introduce another element of unpredictability. See page 49, left-hand column, last paragraph: "Because it is very difficult to predict what portions of an RNA molecule will be accessible in vivo, effective antisense molecules must be found empirically by screening a large number of candidates for their ability to act inside cells."

Having reviewed the full disclosure of Branch, we agree with the examiner that the reference shows that those skilled in the art considered antisense and ribozyme approaches to reducing or eliminating gene expression to be unpredictable, time-consuming, and labor intensive. For this reason, we find Branch to be evidence tending to support the examiner's position that the claims are not fully enabled by the instant specification.

Summary

The evidence of record supports the examiner's position that practicing the claimed method would have required undue experimentation. The rejection of claims 1, 3, 5, 6, and 8 under 35 U.S.C. § 112, first paragraph, is affirmed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

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